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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,968	12/05/2001	Davis T.W. Ng	P05424US1	7842

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EXAMINER

VOGEL, NANCY S

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/004,968

Applicant(s)

NG ET AL.

Examiner

Nancy T. Vogel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6, 13-20 and 24-47 is/are pending in the application.
- 4a) Of the above claim(s) 13, 14, 24, 25 and 32-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 15-20, 26-31 and 43-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

Claims 1-6, 13-20, 24-47 are pending in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Election/Restrictions***

Claims 13, 14, 24, 25, 32-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/19/03.

This application contains claims 13, 14, 24, 25, 32-42 drawn to an invention nonelected with traverse in the paper filed 12/19/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new rejection necessitated by the applicant's amendment filed 6/1/04.

This is a new matter rejection.

The newly added claims 43-47 are drawn to a method of producing a heterologous protein comprising providing a recipient fungi cell possessing a modification of a double disruption of expression of a PMT 1 gene and a PMT 2 gene. The specification does not provide support for this subject matter, since there is no disclosure of a method using a fungi cell possessing this double disruption of expression of the PMT 1 and PMT 2 gene. Therefore, it is considered that claims 43-47 constitute new matter.

### ***Claim Rejections - 35 USC § 103***

Claims 1-6 and 15-20 and 43-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanner et al. (US Patent 5,714,377, previously cited) in view of Strahl-Bolsinger et al. (Biochemi. Biophys. Acta 1426:297-307, 1999, cited by applicant).

This rejection is maintained essentially for the reasons made of record in the previous Office action, in slightly modified form to account for applicant's

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amendment to the claims. Applicant's arguments filed 6/1/04 have been considered, but they are not deemed to be persuasive.

Tanner et al. disclose a method of producing a heterologous protein in a fungi, which is a yeast cell, comprising providing a yeast cell having genetic modification(s) in at least one gene whose expression product is involved in the attachment of a mannosyl residue to the hydroxyl group of seryl or threonyl amino acids (see col. 4, lines 21-25). The method is exemplified with a yeast strain having a mutation in the PMT1 gene, in which O-glycosylation is inhibited (see col. 2 line 52- col. 6, line 62). The transformation method may be the LiAc method or any other technique disclosed in the literature (see col. 5, lines 48-59). A yeast based plasmid may be used (see col. 5, lines 30-47). Tanner et al. disclose that it is advantageous to inhibit O-glycosylation when producing heterologous proteins in yeast since such glycosylation patterns are not present on the native non-yeast proteins, and may result in altered pharmacokinetic properties and biological properties.

The difference between Tanner et al. and the claimed invention is that the PMT gene is PMT 2 (claims 1-6, 15-20), or PMT 1 and PMT 2 (claims 43-47).

However, Strahl-Bolsinger et al. disclose that the proteins encoded by the PMT family of genes in yeast all are mannosyltransferases which are involved in the attachment of a mannosyl residue to proteins. In addition, the reference discloses that the PMT1-6 genes all share homology and activity as protein O-mannosyltransferases (see bottom of page 298), indicating that defects in any of the PMT 1-6 genes results in inhibition of O-glycosylation.

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It would have been obvious to one of ordinary skill in the art to substitute for the yeast cell having a mutation in the PMT 1 gene in the method taught by Tanner et al., with a yeast cell having a mutation in the PMT2, or a mutation in both PMT 1 and PMT 2 genes taught by Strahl-Bolsinger et al., because Tanner et al. teach that it is within the ordinary skill in the art to produce heterologous protein in yeast cells in which O-glycosylation is inhibited by mutating or inactivating any one or more genes encoding an enzyme which is a mannosyltransferase, and Strahl-Bolsinger et al. teach that O-glycosylation can be inhibited by defects in any other PMT 1-6 genes. One would have been motivated to use such multiple or single mutations in the method disclosed by Tanner et al., for the expected benefit of using yeast cells having different defects in O-glycosylation, especially since Strahl-Bolsinger et al. teach that the different PMT encoded enzymes may have different specificities. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

The Declaration under 37 CFR 1.132 filed 6/1/04 is insufficient to overcome the rejection of claims 1-6 and 15-20 and 43-47 based upon USC 103(a) as set forth in the last Office action because:

Applicant has argued that the declaration of Dr. Ng demonstrates that "substituting a PMT gene and arriving at Applicants' claimed invention would not be obvious to one of ordinary skill in the art because the data (Exhibit B) shows

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that a mutation in a PMT 1 gene does not necessarily enhance protein folding when compared to a yeast cell having a PMT 2 mutation or a PMT 1/PMT2 double mutation. Moreover, this demonstrates unexpected superior results over what is disclosed by Tanner as well as Strahl-Bolsinger et al. alone, or in combination" (page 12-13 of the arguments). However, it is maintained that variation in glycosylation and thus proper folding of recombinant proteins with different PMT mutants would have been expected, since it was known in the art that the mannosyltransferase enzymes encoded by the Pmt family of genes in yeast, i.e. encoded by each of the PMT 1 -7 genes, exhibit specificity for particular proteins (see page 301, first column of Strahl-Bolsinger et al.). Applicants further argue that there was no motivation and/or suggestion in the references that they be combined. Applicants state that "Tanner teaches fungal cells carrying a modification in PMT 1 causes the cells to exhibit at least a reduced capacity for O-glycosylating heterologous proteins." (page 13 of the arguments). However, it is maintained that Tanner et al. disclose that the fungal cell may "carry genetic modification in any gene whose expression product is involved in the attachment of a mannosyl residue to the hydroxyl group of seryl or threonyl amino acids". While PMT1 is exemplified by Tanner et al., it is clear that one of skill in the art would have recognized that any of the family of mannosyltransferases, which were known in the art as taught by Strahl-Bolsinger et al., would have been encompassed by the teaching of Tanner et al. Therefore, applicant's arguments are not found convincing.

***Claim Rejections - 35 USC § 112***

Claims 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 and by dependence claims 27-31 lacks antecedent basis for the term "said gene" in the last line, and therefore are vague and indefinite.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
TERRY MCKELVEY  
PRIMARY EXAMINER